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HUMAN BONE MARROW STROMAL CELL PROGENITORS ARE ABLE TO INDUCE DONOR SPECIFIC TOLERANCE AFTER IN UTERO TRANSPLANTATION. G. Almeida-Porada, E. D. Zanjani, VAMC, University of Nevada, Reno, NV.

We have previously employed the human-to-sheep xenogeneic model of in utero transplantation to demonstrate the ability of human hematopoietic stem cells (HSC) to engraft and induce donor specific tolerance after transplantation in utero. Because in this model human stromal progenitors (ST) migrate and engraft in several hematopoietic organs including the thymus, we reasoned that transplantation of human stromal cell progenitors might also be able to induce donor specific tolerance. In this study we co-transplanted each fetus with ST from BM of an adult male human donor (10^6 cells) and 10^5 adult female CD34⁺Lin-Thy⁻ cells. At 4 months post-transplant, after flow cytometric analysis established the chimeric status of the lambs. Mixed Lymphocyte Cultures (MLC) were performed against each one of the donors and a third party human. While the reactivity to a third party human was maintained, a lack of reactivity to both HSC and ST donors was found in 5 out of 6 chimeric lambs. Age matched non-transplanted sheep used as controls were found to be reactive to all three human donors. At 7 months post-transplant tolerant sheep were injected I.V (2×10^6) or S.C. (9×10^6) with T depleted BMNC from either ST donor or HSC donor and evaluated once more by MLC. While sheep injected with HSC acquired the ability to react specifically to the HSC donor independently of the route of boosting at levels similar to the third party human and control sheep, lambs boosted with BMNC from the ST donor remained unresponsive throughout the study period. These results suggest that stroma progenitors are not only able to induce long term donor specific tolerance in sheep fetuses but also that the tolerization mechanism may differ from that of BM HSC.